Many Heavily Treated People With HIV Do Not Need NRTIs

Long-term salvage therapy without NRTIs suppressed HIV in nearly 80% of those who remained in care.

July 11, 2019 By Liz Highleyman

HIV-positive people who have been extensively treated and developed resistance to multiple antiretrovirals can achieve long-term viral suppression with a regimen that does not include nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs), as long as they still have more than two available active drugs, according to a recent study.

NRTIs were the first class of antiretrovirals to be developed, and most people with long-term HIV infection have used one or more of them. But NRTIs are associated with numerous side effects, and if used in regimens that are not fully suppressive, the virus can develop resistance and the meds can stop working. Today, thanks to the availability of newer classes of drugs, including integrase inhibitors, it's easier for highly treatment-experienced people to put together effective combination regimens, raising the question of whether NRTIs are needed.

The OPTIONS study compared NRTI-containing and NRTI-sparing regimens for people who were on treatment but still had a detectable viral load, known as virologic failure.

This Phase III study included 360 participants recruited at more than 60 outpatient medical clinics across the United States between March 2008 and May 2011. About a quarter were women, a third were white and about 40% were Black. The median age was 46. At study entry, they had a viral load of 1,000 or more. They had used a protease inhibitor–based regimen and had either previously used or had evidence of resistance to NRTIs and non-nucleoside reverse transcriptase inhibitors (NNRTIs).

Based on resistance testing, participants were assigned a combined phenotypic susceptibility score that reflected the number of drugs to which their virus remained susceptible. A score of 2 meant they had the equivalent of two remaining active drugs (either two fully active drugs or multiple drugs with partial activity).

Resistance results were used to construct optimized NRTI-sparing regimens with the highest possible score for each individual. These included three or four of the following drugs available at the time: boosted Prezista (darunavir), boosted Aptivus (tipranavir), Isentress (raltegravir,

approved after the start of the study), Intelence (etravirine), Selzentry (maraviroc) and Fuzeon (enfuvirtide).

Participants with scores above 2 were then randomly assigned to omit or add NRTIs along with their optimized regimen. A highly resistant subgroup with lower scores was not randomized, and all received an optimized regimen with NRTIs.

In 2015, the OPTIONS investigators reported that NRTIs-omitted regimens were noninferior to, or at least as good as, regimens that added NRTIs. After 48 weeks of treatment, 70% of people in the NRTIs-omitted group and 74% in the NRTIs-added group had an undetectable viral load, a difference that probably was not driven by chance.

Now, Rajesh Gandhi, MD, of Massachusetts General Hospital, and fellow investigators have reported long-term outcomes two years after randomization.

As described in the Journal of Infectious Diseases, at 96 weeks, 70% of randomized participants in the NRTIs-omitted group and 65% of those in the NRTIs-added group had HIV RNA levels below 200 copies; 61% and 59%, respectively, had less than 50 copies. Looking only at people who remained in follow-up, 79% and 75%, respectively, had a viral load under 200. Both groups saw substantial CD4 cell gains. Younger participants and those who started fewer new antiretrovirals were more likely to experience virologic failure.

In the highly resistant subgroup that was not randomized, the viral suppression rate fell to 53% of the initial group, or 65% of those still in follow-up.

Virologic failure was uncommon after the first 48 weeks, with more than 85% of such cases occurring in the first year. “Even in highly treatment-experienced persons who have drug-resistant HIV-1, once virologic suppression is achieved, it is typically sustained,” the researchers wrote.

Treatment with both NRTIs-omitted and NRTIs-added regimens was generally safe. By 48 weeks, 21% and 24% of participants, respectively, experienced serious adverse events; three events in the NRTIs-omitted group and 13 in the NRTIs-added group were deemed at least possibly related to antiretroviral therapy.

By 96 weeks, there was one death on treatment in the NRTIs-omitted group and 10 in the NRTIs-added group, but these had various causes with “no pattern suggesting a common mechanism,” the researchers said.

People in the NRTIs-omitted group had larger increases in total and harmful LDL cholesterol. Almost everyone in the NRTIs-added group used tenofovir disoproxil fumarate (Viread, also a component of several combination pills), which is known to lower lipids, the study authors noted. Perhaps for this reason, the NRTIs-omitted group had a larger proportion of people with moderate to high cardiovascular risk. Estimated creatinine clearance, a measure of kidney function, declined more in the NRTIs-added group, again potentially attributable to tenofovir. Additional analysis of mitochondrial dysfunction (a known NRTI side effect) and inflammation are under way, according

to the researchers.

Quality of life scores increased significantly in the NRTIs-omitted, NRTIs-added and highly resistant nonrandomized groups, with no notable differences between them in the degree of change.

“HIV-1 salvage therapy can safely omit NRTIs without compromising regimen efficacy or durable virologic response as long as the new regimen contains a sufficient number of active drugs,” the researchers concluded. However, they cautioned, “Younger people and those receiving fewer new antiretrovirals require careful monitoring.”

“Ultimately, including newer agents in salvage regimens, like second-generation integrase inhibitors or drugs against novel targets, [is] likely to improve virologic outcomes even further, leading to sustained virologic suppression in the vast majority of treatment-experienced people with HIV-1,” they wrote.

Click here to read the study abstract.

© 2026 Smart + Strong All Rights Reserved.
http://beta.docker.poz.com/article/many-heavily-treated-people-hiv-need-nrtis